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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,483	03/29/2004	Jun Liu	P2026R1	5594
9157	7590	09/05/2007		
GENENTECH, INC. 1 DNA WAY SOUTH SAN FRANCISCO, CA 94080			EXAMINER KIM, YUNSOO	
			ART UNIT 1644	PAPER NUMBER
			MAIL DATE 09/05/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/813,483	Applicant(s) LIU ET AL.	
	Examiner Yunsoo Kim	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-8,16-25,28-45 and 48-50 is/are pending in the application.
- 4a) Of the above claim(s) 18,19,28-45 and 48-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-8,16,17,20-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>6/25/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 6/25/07 has been entered.

2. Claims 1, 3-8, 16-25, 28-45 and 48-50 are pending.
Upon further consideration, claim 21 is being examined.

Claims 18, 19, 28-45 and 48-50 remain withdrawn from further consideration by examiner 37 CFR.1.142(b) as being drawn to a nonelected species. Claims **1, 3-8, 16, 17 and 20-25** are under consideration.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 3-8 and 20 stand rejected under 35 U.S.C. 102(e) as being anticipated by US2003/0138417 A1, of record as is evidenced by the US 2004/0191243A1, of record, for the reasons set forth in the office action mailed 1/5/07.

The '417 publication teaches a stable isotonic liquid pharmaceutical antibody formulation comprising 50mM histidine buffer, 0.03% polysorbate at pH 6 (Example 8, [104], in particular). The '417 publication further teaches that the pharmaceutical antibody formulation can be used in stabilizing antibody including IgE monoclonal antibody ([0039-42], in particular) at concentration greater than 100 mg/ml (abstract, claims 2-3, in particular) with 200mM of tonicity modifier such as arginine ([0052], in particular).

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In addition, the '417 publication teaches that the isotonic means having osmotic pressure from 270-328 mOsm ([0029], in particular). Moreover, the highly concentrated stable antibody formulation taught in the '417 publication is suitable for various methods of administration, prevents aggregations and increase storage time ([0003], [0013-15], in particular).

Thus, having low turbidity and kinematic viscosity about 50cs and turbidity of 0.30 OD or less mean absorbance in an HP-8453 diode array spectrophotometer at 340-360nm are inherent property of antibody formulation comprising 50 mM Histidine buffer at pH. 6, 200 mM arginine and 0.03% of polysorbate. Therefore, the reference teachings anticipate the claimed invention.

Applicants' arguments filed 6/25/07 have been fully considered but they were not persuasive.

Applicants traversed the rejection based on that there is no specific guidance as in the '417 publication to select arginine-HCl as a tonicity modifier, the examples disclosed in the '417 publication are not enabling and the rejection is improper for "combining the '243 reference".

It is reminded that the purpose of provision of the '243 publication as an evidentiary reference is to rebut the Applicant's argument (filed on 9/21/06) based on that the selection of arginine is from unexpected results (see remark p.10 dated 9/21/06). The '243 publication provides the art recognizes the use of arginine and histidine combination (p. 10-11, ([100, 105], and on p. 10, Table 5, in particular). Therefore, the provision of the '243 publication is not to supply the lacking elements that Applicants assert, because the arginine is taught by the '417 publication.

Applicants further argue that the relying upon teaching of more than 100mg/ml in the '417 publication to anticipate the claimed 120-260mg/ml is not predicative because the viscosity of antibody at high concentrations is viable depending on the antigen specificity based on the Liu et al.

However, the Liu et al. reference supports that there is change in the viscosity with increase of concentration (Fig. 1, in particular) but the reference is silent about the claimed range is enabled or the referenced more than 100mg/ml is not enabled. Moreover, the viscosity is measured in "mPas" which is to measure absolute viscosity while the claimed viscosity is measured in "cs", kinematic viscosity in the Liu reference. According to the specification on p. 22, the conversion factor of "density" is required and

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adequate density information was not provided in the Liu et al. reference. Without this information, it is not clear if the claimed viscosity of cs or less is not enabled by the antibody taught by the '417 publication. Furthermore, the instant specification does not disclose the kinematic viscosity of the antibody. Regardless, the referenced concentration of "more than 100mg/ml" reads on the claimed 120-260mg/ml range.

Applicants further traversed that the presence of NaCl does not result the reduction of viscosity and the examples of '417 publication are not enabling. However, the claimed invention uses "comprising" and it includes other substances such as NaCl, which is to modify tonicity as in the '417 publication. Thus, the reference teachings anticipate the claimed invention.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 16, 17 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2003/0138417 (of record) as is evidenced by the US 2004/109243A1, of record, in view of U.S. Pat. No. 5,994,511 (IDS reference, of record) for the reasons set forth in the office action mailed 1/5/07.

Applicants' arguments filed 6/25/07 have been fully considered but they were not persuasive.

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Applicants traversed the rejection based on that the '417 publication is not anticipatory reference and the combination of teachings is not obvious.

In light of the discussion above in sections 3-4, the '417 publication is a proper anticipatory reference and the combination of teachings remains obvious.

7. Claims 1, 3-8, 16, 17 and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/26909 (IDS reference, of record), in view of U.S. Pat. No. 5,994,511 (IDS reference, of record) for the reasons set forth in the office action mailed 1/5/07.

The '909 publication teaches a stable protein formulation comprising 10 mM histidine, 160 mM arginine-HCl at pH. 7, protein concentration of about 160mg/ml and 0.05% of polysorbate (claims 1-49, in particular).

The '909 publication further teaches that the stable protein formulation adds stability to the protein and enhances therapeutic applicability (p. 5, in particular).

Claims 4-5 are included in this rejection because the concentrations of 180mg/ml or 200 mg/ml are well within the purview of optimization of about 160mg/ml.

In addition, having low turbidity, kinematic viscosity about 50cs and having osmotic pressure from 270-328 mOsm are inherent property of the protein formulation comprising 10 mM histidine, 16 mM arginine-HCl at pH. 7 and 0.05% of polysorbate.

The '909 publication does not teach rhuMabE25 as in claims 16 and 17, article or manufacture with syringe or injection device as in claims 22-25.

However, the '511 patent teaches rhuMabE25 (Table 1, claims 9-10, in particular) composition and an article of manufacture comprising syringes or injection tools (col. 58-59 overlapping paragraph, in particular).

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Therefore, it would have been obvious to one of the ordinary skill in the art at the time the invention was made to stabilize rhuMabE25 as taught by the '511 patent with a formulation comprising a buffer comprising histidine, arginine and polysorbate as taught by the '909 publication.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the '909 publication teaches that a formulation comprising histidine, arginine and polysorbate adds stability to any antibodies and prevents degradation proteins (p. 5, in particular).

From the teachings of the references, one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of the ordinary in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicants' arguments filed on 6/25/07 have been fully considered but they were not persuasive.

Applicants traversed the rejection based on that the claimed rhuMabE25 does not behave as other antibodies at the high concentration range and Liu et al reference is provided.

As discussed above in the sections 3-4, there is no disclosure in the Liu et al. reference that the claimed concentration range of the antibody and having the viscosity of 50 or less is only specific for rhuMabE25. Therefore, the combination of references remains obvious.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1, 3-8, 16, 17 and 20-25 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-13, 22-27, 31-34, 37-42, 48, 51-56, 58 and 59 of U.S. Patent No. 6,875,432 B2 in view of US 2004/109243A1.

As Applicant has requested that this double patenting rejection be held in abeyance until patentable subject matter has been identified in the instant application, the double patenting rejection is maintained.

10. The following new rejections are necessitated by Applicants' amendment filed on 6/25/07.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 1, 3-8, 16 and 17 are rejected under 35 U.S.C. 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "... Hewlett-Packard 8453 diode array spectrophotometer or equivalent" recited in claim 1 renders claim indefinite. It is not clear if the phrase "or equivalent" to mean different diode array spectrophotometer from other vendors or other model numbers from the same vendor. The specification of instant application has not disclosed what is encompassed by the phrase.

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13. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out this invention.

14. Claims 1, 3-8, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The amendment to the claim 1 recites "... Hewlett-Packard 8453 diode array spectrophotometer or equivalent". The Table 1, example 2 of page 70 only discloses "Hewlett-Packard 8453 diode array spectrophotometer" and reciting of "or equivalent" changes the scope of the instant disclosure. The specification does not provide a clear written description for the amendment.

15. No claims are allowable.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yunsoo Kim whose telephone number is 571-272-3176. The examiner can normally be reached on M-F, 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Yunsoo Kim

Patent Examiner

Technology Center 1600

August 21, 2007

A handwritten signature in cursive script, reading "Christina Chan".

CHRISTINA CHAN

SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600